Phencyclidine: An Overview

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The potent psychotomimetic agent phencyclidine, 1-(1-phenylcyclohexyl) piperidine (PCP), is currently found in numerous street drug preparations. The use of PCP, popularly known as “angel’s dust,” “angel’s mist,” “hug,” or “the peace of pill,” is common in the drug community (Rainey & Crowder 1974; Lindren et al. 1969; Hart, McChesney & Grief 1972). It is being sold to the unwary buyer as LSD, cocaine, mescaline and psilocybin, but most frequently as tetrahydrocannabinol (THC) (Lundberg, Gupta & Montgomery 1976). Additionally, the ingestion of PCP sprinkled on a marihuana cigarette has become a popular method for obtaining what has been described as a “high exceeded only by that obtained with cocaine” (Garey & Weisberg 1977; Boyd 1974). This mixture empirically derived by drug users appears to have a scientific basis. Recent findings have demonstrated that Δ9-THC, the principal psychoactive component of marijuana, potentiates the effects of PCP (Murray & Craighill 1976). The increasing use of PCP and its nefarious sales as other compounds has resulted in a dramatic increase in the number of PCP overdoses encountered by the medical community. A better understanding of this drug would, therefore, benefit not only those who use it, but those who are responsible for medical management of its toxic effects.

SYNTHESIS AND CHEMICAL PROPERTIES

The synthesis of PCP involves the use of benzene, piperidine and p-toluenesulphonic acid. Additionally, ether, cyclohexanol, phenol-magnesium-bromide, isopropyl alcohol, hydrochloric acid, ammonium chloride, ammonium hydroxide and phenol-lithium are used at various stages of its preparation (Maddox, Godefroi & Parcell 1965). The failure to remove these toxic compounds from the final preparation appears to be responsible for some of the severe physiological effects such as abdominal cramps, blood emesis, convulsions, coma and death, sometimes seen with the ingestion of PCP (Lampe 1971). With proper care, however, a relatively pure (99%+) preparation can be achieved and the toxic effects diminished.

In order to ensure its solubility, PCP is usually prepared as the hydrochloric salt. The final product appears as a white granular powder, which is freely soluble in water and ethanol. If one is aware of this fact, it becomes quite simple to distinguish between PCP and THC, as both are soluble in ethanol, but only PCP is water soluble. Pure PCP has a molecular weight of 243.38 and a melting point of 234-236°C. It is a relatively stable compound, both in the crystallized form or in solution.

HISTORY

The search for an efficient intravenous anesthetic led to a series of cyclohexylamine derivatives being synthesized and studied in the laboratory. The first of these was PCP, which was marketed under the name Sernyl. During preliminary animal studies, it was observed that during surgery, the animal had its eyes open and looked about unconcernedly (Greifenstein et al. 1958). This blockade of sensory input and lack of profound physiological effects on other systems...
suggested that PCP works almost exclusively on the nervous system and, in particular, on the higher sensory integrative functions of the central nervous system. It was hypothesized that PCP and its derivatives produced a blocking effect of sensory input without concomitant sleep and without significant depression of respiration and circulation.

The biochemical and pharmacological properties of PCP tend to support this hypothesis. PCP has been shown to affect the catabolism, steady-state levels, and turnover rates of most of the putative neurotransmitters in the CNS. Although Ban (1969) has classified PCP as an anticholinergic agent, Maayani et al. (1973) have shown that it is a competitive inhibitor of acetylcholinesterase (ACHE). The psychotomimetic effects of PCP, however, appear to be more closely related to its anticholinergic effects than its ability to block ACHE activity (Maayani et al. 1973). Additionally, in the peripheral nervous system, PCP blocks the reuptake of norepinephrine (NE) into postganglionic nerve terminals and has anticholinergic properties at muscarinic receptors (Nedergaard 1973; Maayani et al. 1974). It is possible that the multiple effects of PCP could explain the wide range of symptomatology and adverse reactions seen with PCP. Other studies have shown that the metabolism of serotonin (5-HT), NE and dopamine (DA) are affected by PCP (Leonard 1972; Hitzemann, Loh & Domino 1973; Domino & Wilson 1972). Garey and Heath (1976) have recently demonstrated that PCP is a competitive inhibitor of DA uptake in the striatum and NE uptake in the hypothalamus. In a pharmacokinetic sense, this property is similar to amphetamine and may be responsible for some of the physiological and psychological similarities between amphetamine and PCP. The psychopharmacological similarities between PCP and amphetamine can be observed in rats which have been unilaterally lesioned in the substantia nigra. Both compounds induce ipsilateral turning in these animals, an effect which is potentiated by cholinomimetics, reduced by anticholinergics and blocked by haladol (Finnegan, Kanner & Meltzer 1976; Klawans et al. 1972). The authors pointed out, however, that there is a qualitative difference between PCP and amphetamine-induced ipsilateral turning, a difference which was explained by the more potent anticholinergic effects of PCP (Finnegan, Kanner & Meltzer 1976). Since PCP has both anticholinergic and anticholinergic properties, it seems reasonable to suggest that the physiological and psychological response to PCP is a result of complex drug interactions with those systems in both the peripheral and central nervous systems. Acute psychotic states have been postulated to result from an imbalance between the cholinergic and dopaminergic systems in brain centers involved with the control of emotional expression (Stein 1973). The unique psychopharmacological properties of PCP tend to support such a model and supply at least a working model as to the biochemical basis of drug-induced psychosis.

In 1958, Greifenstein investigated Sernyl as a human anaesthetic and reported that, at dosages of more than 0.5 mg/Kg i.v., the patients became agitated; and at 1 mg/Kg, rigidity occurred, followed by catatonia and convulsions. A dosage of .25 mg/Kg was found to be satisfactory for anaesthetic use and was used in 34 patients undergoing surgical procedures. During this procedure, the majority of patients were quiet, but several became agitated and confused, although this may have been related to inadequate analgesia. Other effects included: 1) elevation of blood pressure in all; with some patients having an accompanying increased heart rate, hypotension and bradycardia were not observed; 2) muscle relaxation was not achieved and in some cases, increased muscle tone and hyperactive deep tendon reflexes were observed; 3) vertical and horizontal nystagmus; 4) bilateral ptosis with impaired pupillary reactivity; 5) increased minute and tidal respiratory volume; 6) impaired visual identification; 7) pin prick was appreciated but was no longer painful and other sensory modalities were also decreased, i.e., the impairment of proprioception was perhaps responsible for the ataxia; 8) EEG was characterized by diffuse slow wave pattern with suppression of the fast activity as contrasted to barbiturate in which fast (beta) rhythm is accentuated.

Post-operatively, the patients were initially dissociated and euphoric, and their behavior resembled alcohol intoxication, and this lasted three to 19 hours following the operation. Not infrequently, the patients had violent emergence reactions during which they became agitated and combative. These states were successfully treated with meperidine or morphine. When their attention and consciousness cleared, they had retro- and antegrade amnesia, although awake in the operating and recovery room. For up to 24 hours, the patients complained of dizziness with true rotational component and nystagmus. Because of these reactions, the use of Sernyl in anaesthesia was discontinued in humans and is now used only as an anaesthetic in primates. Other derivatives of this group, such as cyclohexamine, were also tried in humans, but again, severe psychological postoperative disturbances were noted.

Davies and Beech, in 1960, administered Sernyl to 12 normal volunteers (0.75 mg/Kg), and reported that,
unlike LSD, the acute effects of PCP begin almost immediately and are over within an hour, although general malaise persisted for several hours. No hallucinations were reported, unlike LSD or mescaline, but dramatic changes in perception (i.e., distortion of body image, depersonalization, disruption of time perception and slowness and/or difficulty in concentrating or remembering) were seen. These investigators suggested that these symptoms were similar to certain primary symptoms of schizophrenia and, therefore, may have a similar basis. In normal volunteers, the following psychological and psychomotor parameters were altered following PCP administration: 1) decreased speed in performing rapid repetitive motor tasks, including tapping a stylus upon a motor plate for a ten second period; 2) lowered rate of flicker to perceive visual fusion; 3) poor estimation of time interval; 4) decreased immediate recall and concreteness of thought in proverb interpretation. Physical findings which occurred included decreased proprioception, pain and temperature discrimination, pupillary dilation with decreased reactivity, horizontal and vertical nystagmus, increased tone and tendon reflexes with clonus but no Babinski sign, fine sustentation tremor, dry mouth or lips.

In other studies (Luby et al. 1959; Ban et al. 1961), PCP was administered to normals as well as schizophrenics. Both groups reported similar findings, i.e., the activations of primary symptoms of schizophrenia to a greater degree than either mescaline or LSD. The drug did not normally produce hallucinations. Patients with chronic schizophrenia appear to be highly resistant to LSD and mescaline and are able to tell the difference between the effects of these two drugs and the symptoms of their illness. In contrast, PCP exaggerated their associational defect and frequently their inappropriate affectivity. It also resulted in feelings which were more characteristic of the acute and earlier stages of schizophrenia. These changes lasted for weeks and suggest that PCP may act on some fundamental aspect of this disease. Distortion of body images and an intense fear of dying were the more characteristic symptoms observed, the same as reported for normal volunteers receiving this drug. The use of this drug in treating psychiatric illness, particularly schizophrenia, was not recommended by any of these investigators. From the foregoing studies, one may conclude that the only use of PCP in relationship to human subjects is that of a research tool to study the causes of schizophrenic-like symptoms that PCP induces.

**PREVALENCE**

The use of PCP as a street drug, either alone or in combination with amphetamine, cocaine, mescaline, LSD or marijuana has been confirmed by numerous studies in which street drug samples were analyzed. PCP, for example, was detected in 184 of 237 samples submitted to the Department of Chemistry at Kansas University between August, 1970 and January, 1972 (Hart et al. 1972). During another two-month period, PCP was detected in 195 samples submitted for analysis (Anonymous 1973), and in Philadelphia, PCP was found in eight of 20 samples of “mescaline” (Schnell & Vogel 1971). In Massachusetts, 10 of 20 samples analyzed contained PCP (Linden, Lovejoy & Costello 1975). The widespread use of phencyclidine, either knowingly or unknowingly, has increased the number of overdoses reported in the medical literature. The frequency of such overdoses has prompted reports suggesting that “PCP abuse has become increasingly common and should be considered in patients with unexplained psychosis, dystonic reactions, status epilepticus or coma” (Tong et al. 1975). It was also reported that between the fall of 1973 and the spring of 1974, 11 male patients were admitted to a Washington, D.C. hospital suffering from PCP-induced psychosis and resulted in a report at the American Psychiatric Association meetings entitled “Epidemic of Psychosis Caused by Use of Angel’s Dust” (Luisada & Reddick 1975). Numerous other examples of one or multiple cases of PCP overdose can be found in current medical literature (Linden, Lovejoy & Costello 1975; Tong et al. 1975; Faume et al. 1976).

**MEDICAL FINDINGS**

In reviewing the cases reported, a wide variety of symptomatology emerges which appears to be dependent on: 1) social setting; 2) dose and route of administration; 3) other drug involvement; and 4) personality traits. Behavioral anomalies most frequently reported are agitation, anxiety, disordered thought processes, body image disturbance, euphoria, depersonalization, and occasionally auditory and/or visual hallucinations. Agitation is frequently seen following diminution of the acute symptoms. The prevalence of hallucinations is much less frequent with PCP than with other drugs known to cause a toxic delirium, and those that are reported are more suggestive of an illusionary state related to the body image disturbance, rather than to true hallucinations. In most cases, there is minimal paranoid ideation and the patient is not anxious, combative or hostile. If these are present, an underlying psychiatric disorder or mixed drug reaction should be suspected. Luisada and Brown (1976) described phencyclidine psychosis in the more severely affected users and considered this to consist of three phases.
characterized by: 1) initial violent psychotic behavior with prominent paranoid ideation, lasting up to one week; 2) restless and combative delirium without violence for one week; 3) rapid personality reintegration and restoration of normal thought processes and associations. Neurological symptoms that occur in almost all patients are nystagmus (rotary, horizontal or vertical), variable pupil size with depressed light reflex, diminished pain and temperature response, ataxia, slurred speech, tremors, increased deep tendon reflexes, clonus and muscle weakness. At higher doses, dystonic reactions, including opisthotonic posturing, torticollis and facial grimacing have occurred. At doses which approach or exceed the anaesthetic level, respiratory depression, coma, decreased muscle tone and status epilepticus have been reported. In some instances, this had led directly to death (Burns et. al. 1975).

PCP appears to block selected sensory inputs. However, PCP administered to volunteer subjects in isolation chambers results in a feeling of “utter nothingness”. Upon emergence from the chamber, distorted perception, prolonged reaction time and marked depression of the proprioceptive senses occurred, but the psychological disturbances previously noted were absent or greatly reduced (Cohen et. al. 1960). It appears, therefore, that exteroceptive input is required to produce the psychotomimetic effects seen with PCP. Another factor which suggests that exteroceptive input is important in the symptomatology of PCP is that, unlike bad LSD trips, attempts to “talk down” a bad PCP trip cause intensification of the symptoms (Cohen et. al. 1960; Stein 1973). In examining these findings, it would be hypothesized that, after an initial anaesthetic effect, even if subclinical, the exteroceptive sensory inputs to the CNS become “super-sensitive” and may be responsible for the overt psychotomimetic effects observed clinically.

Other factors, such as age, sex and personality, also appear to function in the production of psychotomimetic symptoms following PCP ingestion. Young adult males appear to be more susceptible than females or older age groups (Johnstone, Evans & Bugel 1959). At anaesthetic doses, not all patients became psychotic or displayed behavioral problems. In fact, only about 20 to 30 percent display these symptoms, even after anaesthetic doses. Several reports have shown that the disinhibitory potential of PCP and the activation of psychopathology results in the quiet, undeactive person becoming stuporous and catatonic, and the overactive person becoming agitated and restless (Greifenstein et. al. 1958; Gershon & Olariu 1960). This intensification of underlying personality traits is comparable to the reported intensification of primary symptoms, i.e., inappropriate affect and associated defects in schizophrenics given PCP. Apparently, the drug tends to amplify the basic processes determining the mental status of the user.

**TREATMENT**

Because PCP is rapidly absorbed, removal with lavage or emetic is usually unsuccessful. Recently, removal of PCP by continuous gastric drainage following acidification of the urine by ammonium chloride has been suggested (Aronow & Done 1976). The combination of PCP with other drugs makes the management of overdoses a critical problem. Fatal status epilepticus has been reported in which both PCP and barbiturates were found (Kessler et. al. 1974). The combination can also lead to respiratory collapse. Warnings have been issued not to use phenothiazines in treatment of overdoses, since the drug combination may have contained belladonna, which would lead to an atropine (anticholinergic) crisis, which may require treatment with 2-4 mg phystostigmine (Taylor, Maurer & Tinklenberg 1960).

To compound the problem in such cases, the anti-adrenergic effect of the phenothiazine may cause hypotension and bradycardia. In cases where PCP was known to be the only drug involved, chlorpromazine was claimed to be an effective antidote by some, while others felt that, while it was beneficial, PCP-induced psychosis did not respond to chlorpromazine as quickly as schizophrenia (Luisada & Reddick 1975; Balster & Chait 1976). Haloperidol has been suggested as the drug of choice in treating PCP overdoses, since it modifies the PCP-induced psychosis with less change of inducing an atropine crisis in the event of anticholinergic involvement (Gershon & Olariu 1960). A problem that one must be aware of, however, is that PCP may cause dystonic reactions which may be exacerbated by haloperidol. Succinate has also been suggested as an antidote to PCP, but reports on this treatment have been conflicting (Gershon & Olariu 1960; Newbauer, Sundland & Gershon 1966). With the multiple properties of PCP, it is probable that no single drug will be effective in treating all symptoms seen in cases of PCP overdose. At the present time, supportive medical care, a quiet but reassuring environment, diazepam (Valium) to reduce the increased muscle tone (spasticity) and opisthotonus, Benadryl for the dystonic reaction, and Haldol for the acute psychotic reactions are suggested. Psychiatric intervention should be started only after the agitated state is controlled and the patient is clinically stable.

The presence of PCP can be confirmed by thin-layer chromatography or gas chromatograph-mass spectral analysis.

*Journal of Psychedelic Drugs* 283 Vol. 9(4) Oct-Dec, 1977
SUMMARY

The quantity of PCP necessary to induce a "trip" or to produce toxic effects is quite similar, and its effect on individuals are quite variable. Of further complexity is the fact that PCP is often sold as other drugs, such as THC. Because of the widespread use of this drug, it should be a part of the differential diagnosis in any psychotic presentation, especially if a drug psychosis is suspected. Since it has a much more devastating effect on the nervous system than any of the hallucinogens, it may result in status epilepticus, respiratory arrest or coma. In these respects, PCP is perhaps the most dangerous drug found in the streets today. One can argue, of course, that the hard narcotics are not only more dangerous in the physical sense, but are addicting as well, and therefore are much more hazardous than PCP. It should be pointed out, however, that narcotic addicts are, in general, more experienced in the use of drugs than are the users of PCP and, therefore, less likely to experience bad trips or overdoses than a naive drug user of the other street preparations. Regardless of the theoretical arguments concerning the relative merits of any street drug, PCP must be considered as a potentially lethal drug when used in the street form, and the user would be aware of the possible consequences of its use; from the number of reports in the medical literature, this is not the case.

REFERENCES


Garey, R.E. & Weisberg, I.A. 1977. Personal communications with patients using PCP.


